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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/670,096	09/26/2000	Linda S. Mansfield	MSU 4.1-526	7494

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EXAMINER
BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
1645	6

DATE MAILED: 07/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/670,096	MANSFIELD ET AL.	
	Examin r	Art Unit	
	Padmavathi v Baskar	1645	

-- Th MAILING DATE of this communication appears on the cover sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. The amendment filed on 3/25/02 has been entered into the record. Claims 1 and 21 have been amended. Claims 1-3 and 21-22 are pending in the application.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

3. In view of amendment to the claims 1 and 21, the rejection under 35 U.S.C. 112, second paragraph for claims 1-3 and 21-22 is withdrawn.

Rejections Maintained

4. The rejection of claims1-3, 21 and 22 under 35 U.S.C. 112, first paragraph (scope) is maintained as set forth in the previous office action.

Claims1-3, 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition antibodies, does not reasonably provide enablement for a vaccine and a method for providing protection to an individual infected with S.neurona infection comprising antibodies which are against 16 ±4 kD and 30 ±4 antigen of Sarcocystis neurona. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a vaccine and a method for providing protection to an individual infected with S.neurona infection comprising antibodies which are against 16 ±4 kD and 30 ±4 antigen of Sarcocystis neurona both of which are specific to S.neurona.

The instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is a vaccine and a method for providing passive protection to an individual infected with S.neurona infection comprising antibodies, which are against 16 ±4 and 30 ±4 kD antigen of Sarcocystis neurona. The method for providing passive immunity thus requiring an *in vivo* enablement for intended use of the antibodies (i.e., pharmaceutical or therapeutic, page 15 of specification). Pharmaceutical uses include the *in vivo* diagnosis, prevention, treatment, or cure of a disease or condition. The specification discloses that the antibodies of the instant claims are intended for use as "pharmaceutical /therapeutic compositions" useful for treating/preventing S.neurona infection in an equid. The specification,

however, provides no working examples demonstrating (i.e., guidance) enablement for any *in vivo* uses of the claimed antibodies. The treatment /prevention of S.neurona infection in an equid with antibodies is highly complex and unpredictable. As taught by the prior art, Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838) it is apparent that not all antibodies generated to an antigen will neutralize the protein. Further, Liang *et al.* teach that '[A] although S. neurona was sensitive to specific antibodies, a 10-min exposure to antiserum was required to yield a significant reduction in parasite production. This may partially explain why protective antibodies to some apicomplexan parasites are effective *in vitro* but not *in vivo*. Newly released parasites are exposed to serum for a shorter time *in vivo*, and the access of neutralization-sensitive epitopes to antibody may be limited' (page 1837, right column, 3rd paragraph). Further, Liang *et al.* teach that cytotoxic T-cells are ineffective in attacking merozoites migrating to the central nervous system, and conclude while Sn 16 kD and Sn 14 kD antigens are expressed *in vivo,* further investigation of these candidate antigens is necessary for inclusion in a vaccine (page 1837, bridging paragraphs of first and second columns). The results of and conclusion by Liang *et al.* clearly indicates that *in vitro* data does not necessarily correlate to or be extendable to *in vivo*. Whether the claimed vaccine prevents infection in an equine or prevents the spread of S. neurona to the nervous system and CSF is not known and needs to be experimented. The specification does not provide evidence that the vaccine (passive immunization with antibodies) either prevents the equid from infection or prevents the spread of *S. neurona* to the nervous system and CSF, which support such an assertion. Furthermore, it is unclear whether such an immunotherapy can be used to treat an ongoing infection or whether it is effective only in terms of prevention. The physiological art in general is acknowledged to be unpredictable (MPEP 2164.03). In light of the teachings of Liang *et al* that the ability of an antibody to function *in vitro* does not correlate to function *in vivo,* the instant specification has not given the necessary teaching to provide a nexus between the proposed antibody and a functional prophylactic vaccine. In addition, the specific antibodies which bind to 16kD and 30 kD antigen required to practice the claimed invention are not disclosed in the instant specification, nor the art of record. The high degree of unpredictability associated with the claimed method underscores the need to provide teachings in the specification that would provide the artisan with specific treatment regimens that achieve a therapeutic benefit; however, the specification does not provide such guidance and fails to provide the necessary guidance. Further, as indicated by Liang *et al.*, one cannot predict the activity of an antigen for use in a vaccine from *in vitro* data. While the immunological data of record strongly suggests that the antigens are cell surface antigens, there is no function ascribe to these antigens and thus, no nexus between immunization of animals with antibodies to the claimed antigens and targeting these antigens and disrupting any activity which would result in protective prophylactic effect required of a vaccine. Without necessary specific guidance in the specification and the lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

Applicants' arguments filed on 3/25/02 have been fully considered but they are not deemed to be persuasive.

Applicant states that the cited Liang's art suggests that antibodies against 14kD and 16kD antigen would be efficacious in inhibiting disease caused by S.neurona and applicant's

claimed vaccine which consists antibodies against 16 kD and 30kD antigens is consistent with the teaching of Liang. It is the examiner position that certainly Liang et al disclose that antibodies to 14kD and 16kD antigen neutralize the merozoites and suggests that these surface antigens are important vaccine candidates. However, Liang et al show that the antibodies to 30kd antigen are non-neutralizing (in vitro neutralization assay). Therefore, antibodies to against 16 kD and 30kD antigens would inhibit the ongoing infection in horses is unpredictable since newly released parasites exposed to the antibodies for a short-time and the efficacy of the antibodies in an infected horse needs further experimentation. Further, applicant has not provided any evidence to show that the antibodies to16kD and 30kD antigens are protective in animals infected with S.neurona.

New Rejection

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated Liang et al 1998 (Infection and Immunity; 66 (5) 1834-1838).

The claims are directed to a vaccine for providing passive protection comprising antibodies, which are against a 16 $\pm$4 kD antigen and 30 $\pm$4 kD antigen of S.neurona both of which are specific to S.neurona.

Examiner is viewing vaccine comprising antibodies as a composition comprising antibodies.

Liang et al 1998 (see figure 1 and 2) disclose equine antibodies (i.e., serum antibodies are polyclonal antibodies) which are against a 16 $\pm$4 kD antigen and 30 $\pm$4 kD antigen of

S.neurona both of which are specific to S.neurona (see binding pattern of antibodies to Sn 30 kD and Sn16 kD antigens in figure 1 E). In the absence of evidence to the contrary the disclosed prior art antibodies and the claimed antibodies are the same. Since the Office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430.

A recitation of the intended use of the claimed invention (i.e., vaccine for providing passive protection comprising antibodies) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Status of Claims

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

7/4/02

MARK NAVARRO
PRIMARY EXAMINER